

REMARKS:

In the Office Action dated August 10, 2007, claims 1-14, in the above-identified U.S. patent application were rejected. Reconsideration of the rejections is respectfully requested in view of the above amendments and the following remarks. Claims 1 and 3-14 remain in this application, claim 2 has been canceled and new claim 15 has been added to the application.

Claims 1 and 3 were rejected under 35 USC §102(b) as anticipated by Makishima (WO 96/33215) in view of U.S. Patent No. 7,235,527. Claim 1 has been amended to indicate that bone morphogenetic factor human MP52 and mannitol are mixed at a weight ratio of 1: 5-50. Neither of the cited references disclose a weight ratio of 1: 5-50. In view of this amendment, applicants request that this rejection be withdrawn.

Claims 1-7 and 12-14 were rejected under 35 USC §103(a) as unpatentable over Makishima (WO 96/33215) and U.S. Patent No. 7,235,527 in view of Ron (U.S. Patent No. 5,171,579) and Avis. The present claims indicate that the aqueous solution containing MP52 and mannitol is filtered prior to lyophilization. The addition of mannitol to the aqueous MP52 solution results in a higher concentration of MP52. The addition of mannitol has unexpectedly been found to produce an MP52 solution with good solubility and no aggregates. This allows the MP52 to be filtered without losing large amounts of MP52 due to the retention of aggregates by the filter. If lyophilization is carried out without mannitol or filtering, the aggregates would be lyophilized and maintained after redissolution. These aggregates could interfere with the administered dose and injection. The Avis reference provides a general discussion of lyophilization but has nothing to do with proteins in particular and thus does not suggest the use of mannitol and filtering to prevent aggregates of MP52. Ron does not cure the deficiencies in Avis as Ron does not suggest that mannitol is suitable for the use in a

filtered and lyophilized product of MP52 either. Makishima (WO 96/33215) and U.S. Patent No. 7,235,527 do not cure the deficiencies in Ron and Avis as neither Makishima reference suggests or discloses the addition of mannitol combined with filtration to avoid aggregates. In addition, neither Makishima reference suggests or discloses a weight ratio of 1: 5-50. Since none of the cited references individually or in combination suggest the use of mannitol and filtration to produce a lyophilized composition without aggregates, applicants request that this rejection be withdrawn.

Claims 7-14 were rejected under 35 USC §103(a) as unpatentable over Makishima (WO 96/33215) and U.S. Patent No. 7,235,527 in view of Ron and Avis further in view of Chang. Chang does not suggest the use of mannitol and filtration to prepare a lyophilized MP52 composition and thus Chang does not cure the deficiencies in Makishima (WO 96/33215) and U.S. Patent No. 7,235,527 in view of Ron and Avis. There is no suggestion in any of the cited art that mannitol can be used to prevent aggregates which allows the MP52 solution to be filtered prior to lyophilization. In view of the above discussion, applicants request that this rejection be withdrawn.

Claims 7-10 and 12-14 were rejected under 35 USC §103(a) as unpatentable over Makishima (WO 96/33215) and U.S. Patent No. 7,235,527, Ron and Avis in view of Chang, further in view of Hansen, in light of the MeSH definition of "poloxamer". As discussed above, the combination of Makishima (WO 96/33215) and U.S. Patent No. 7,235,527, Ron, Avis and Chang, does not suggest that mannitol should be used prior to filtration when lyophilizing MP52. Hansen is cited only for the disclosure of surfactants for stabilization of freeze-dried proteins and does not cure the deficiencies in Makishima (WO 96/33215) and U.S. Patent No. 7,235,527, Ron, Avis and Chang regarding the use of mannitol with MP52 in a filtered,

lyophilized composition. In view of the above discussion, applicants request that this rejection be withdrawn.

Applicants respectfully submit that all of claims 1 and 3-15 are now in condition for allowance. If it is believed that the application is not in condition for allowance, it is respectfully requested that the undersigned attorney be contacted at the telephone number below.

In the event this paper is not considered to be timely filed, the Applicant respectfully petitions for an appropriate extension of time. Any fee for such an extension together with any additional fees that may be due with respect to this paper, may be charged to Counsel's Deposit Account No. 02-2135.

Respectfully submitted,

By /Monica Chin Kitts/

Monica Chin Kitts
Attorney for Applicant
Registration No. 36,105
ROTHWELL, FIGG, ERNST & MANBECK
1425 K. Street, Suite 800
Washington, D.C. 20005
Telephone: (202) 783-6040

MCK/